REMARKS

Applicants have cancelled claim 2 without prejudice expressly reserving the right to pursue the subject matter of the cancelled claim in one or more subsequent applications. Applicants have also cancelled non-elected claims 3-5, 9 and 12-17 reserving the right to pursue the subject matter of the cancelled claim in one or more subsequent applications.

Applicants have amended claim 1 to recite that the Par-4 is a rat prostate apoptosis responsive-4 protein fragment. Support for this amendment is found. e.g., in: paragraph [00103], which discloses that the 332 amino acid protein Par-4 has two putative nuclear localization sequences, NLS1 (amino acid 20-25) and NLS2 (amino acid 137-153) that are conserved in human, ***rat*** and mouse Par-4; paragraph [0043] for the first identification of the Par-4 gene and cites to Sells et al. (Cell growth Differ., 1994, Vol. 5, pages, 457-466)(enclosed). Support is also found in Applicants' Example 1 which describes the construction of Par-4 deletion mutants and cites to pCB6^{+}-Par-4 plasmid described in Johnstone et al. (Molecular and Cellular Biology 1996 Vol. 16(12):6945-6956)(enclosed), which encodes the 332 amino acid rat Par-4 protein, (see Materials and Methods first paragraph, second sentence) and recites the sequence of the 332 amino acid rat Par-4 protein (see Figure 1).

Applicants have also amended claim 1 to recite that the Par-4 protein fragment is selected from the group of consisting of amino acids 1-204, 137-221, 137-213, 137-198 and 137-195 of the Par-4 protein. Support for this amendment is found e.g., in original claim 2 and in paragraph [0056].

Applicants have amended claim 6 to claim an isolated fusion polypeptide comprising a Par-4 fragment selected from the group consisting of amino acids 1-204, 137-221, 137-213, 137-198 and 137-195 of Par-4 protein. Support for this amendment is found e.g., in paragraphs [0023], [0027], [0028] and [0102].

Applicants have amended claim 24 to recite a pharmaceutical composition for the treatment of cancer, comprising an isolated and purified Par-4 protein selected from the group consisting of amino acids 1-204, 137-221.137-213, 137-198 and 137-19 of the Par-4 protein, and a pharmaceutically acceptable diluent, carrier or excipient. Support for this amendment is found e.g. in paragraph [0022].

Claim 1 is objected to for reciting the tumors are resistant to Par-4 and for missing the word –at—prior to "least one amino acid" and prior to "naturally produced Par-4". These objections are obviated in view of the amendments to Claim 1 to recite that the tumors are resistant to apoptosis by Par-4 and to delete the phrases "least one amino acid" and "naturally produced Par-4".

Claim 2 stands rejected under 35 U.S.C. §112, second paragraph for being indefinite in that the metes and bounds of "1-204, 137-221, 137-213, 137-198 and 137-195" are purportedly unclear. Applicants respectfully disagree.

Throughout the application Applicants describe the protein fragments with reference to the 332 amino acid Par-4 protein. The 332 amino acid Par-4 protein was known to be rat Par-4 protein by those of skill in the art, see e.g., Johnstone et al. 1997 and NCBI Genbank, locus Q62627 (the *Rattus norvegicus* Par-4 protein)(copy enclosed). One of ordinary skill in the art would readily

understand from the phrase "1-204, 137-221, 137-213, 137-198 and 137-195" in claim 2, which fragments of the 332 amino acid rat Par-4 protein are encompassed, without more instruction. Nonetheless, Applicants have cancelled claim 2 without prejudice and thus have obviated the rejection.

The claims stand rejected under 35 U.S.C. §112, first paragraph for purportedly failing to comply with the written description requirement. In particular the Examiner contends that the term "Par-4s" is not supported by the specification. Applicants amended claims do not recite the term "Par-4s" and thus Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §112, first paragraph for purportedly failing to comply with the written description requirement.

Claims 1, 2, 6 and 24 stand rejected under 35 U.S.C. §112, first paragraph for purportedly lacking enablement. In particular, the Examiner acknowledges that the application is enabling for "an isolated modified rat Par-4 wherein the modified Par-4 is selected from the group consisting of fragments 1-204, 137-221, 137-213, 137-198 and 137-195 ..." but that the specification does not reasonably provide enablement for any other embodiment. Although Applicants respectfully disagree, Applicants have amended claim 1 such that the modified Par-4 protein is a rat prostate apoptosis responsive-4 (Par-4) protein fragment and is selected from the group consisting of amino acids 1-204, 137-221, 137-213, 137-198 and 137-195 of the Par-4 protein.

In view of the amendments to the claims and the foregoing remarks applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §112, first paragraph.

Claims 1, 6 and 24 stand rejected under 35 U.S.C. §102(b) for purportedly being anticipated by Guo et al. (Nature Medicine, 1998, pages 957-962). Applicants' claims recite that the modified rat Par-4 protein consists of particular fragments of the rat Par-4 protein, which are not disclosed by Guo. As such Guo does not anticipate Applicants' invention as claimed. As such, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §102(b).

Claim 6 stands rejected under 35 U.S.C. §102(e) for purportedly being anticipated by Darrow et al. (US 2006/0141451). In view of the amendments to the claim Applicants request that the Examiner reconsider and withdraw the rejection.

As amended claim 6 recites an isolated fusion polypeptide comprising a modified rat Par-4 protein wherein the modified rat Par-4 protein is selected from a particular group of rat Par-4 protein fragments. Darrow et al. fails to teach the particular fragments recited in applicants claims and thus does not anticipate the claimed invention.

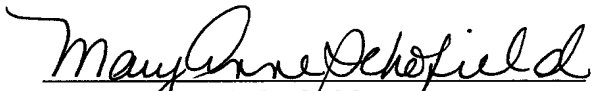
In view of the amendments to the claims and the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of claim 6 under 35 U.S.C. 102(e).

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 104072.B000118).

Respectfully submitted,

June 9, 2008



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1: Q62627. Reports PRKC apoptosis WT...[gi:66773786]

BLink, Conserved Domains, Links

Comment Features Sequence

```
LOCUS       Q62627                    332 aa            linear   ROD 15-JAN-2008
DEFINITION  PRKC apoptosis WT1 regulator protein (Prostate apoptosis response 4
            protein) (Par-4) (Transcriptional repressor Par-4-like protein
            PAWR).
ACCESSION   Q62627
VERSION     Q62627.1  GI:66773786
DBSOURCE    swissprot: locus PAWR_RAT, accession Q62627;
            class: standard.
            created: May 24, 2005.
            sequence updated: Nov 1, 1996.
            annotation updated: Jan 15, 2008.
            xrefs: U05989.1, AAA16492.1, NP_277020.1
            xrefs (non-sequence databases): UniGene:Rn.9127, IntAct:Q62627,
            Ensembl:ENSRNOG00000005917, GeneID:64513, KEGG:rno:64513,
            RGD:69065, ArrayExpress:Q62627, GermOnline:ENSRNOG00000005917
KEYWORDS    Apoptosis; Coiled coil; Cytoplasm; Nucleus; Phosphoprotein;
            Transcription; Transcription regulation.
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Muridae; Murinae; Rattus.
REFERENCE   1  (residues 1 to 332)
  AUTHORS   Sells,S.F., Wood,D.P. Jr., Joshi-Barve,S.S., Muthukumar,S.,
            Jacob,R.J., Crist,S.A., Humphreys,S. and Rangnekar,V.M.
  TITLE     Commonality of the gene programs induced by effectors of apoptosis
            in androgen-dependent and -independent prostate cells
  JOURNAL   Cell Growth Differ. 5 (4), 457-466 (1994)
   PUBMED   8043520
  REMARK    NUCLEOTIDE SEQUENCE [MRNA], AND INDUCTION.
            TISSUE=Prostate
REFERENCE   2  (residues 1 to 332)
  AUTHORS   El-Guendy,N., Zhao,Y., Gurumurthy,S., Burikhanov,R. and
            Rangnekar,V.M.
  TITLE     Identification of a unique core domain of par-4 sufficient for
            selective apoptosis induction in cancer cells
  JOURNAL   Mol. Cell. Biol. 23 (16), 5516-5525 (2003)
   PUBMED   12897127
  REMARK    DOMAIN SAC, MUTAGENESIS, AND SUBCELLULAR LOCATION.
REFERENCE   3  (residues 1 to 332)
  AUTHORS   Gurumurthy,S., Goswami,A., Vasudevan,K.M. and Rangnekar,V.M.
  TITLE     Phosphorylation of Par-4 by protein kinase A is critical for
            apoptosis
  JOURNAL   Mol. Cell. Biol. 25 (3), 1146-1161 (2005)
   PUBMED   15657440
  REMARK    PHOSPHORYLATION.
REFERENCE   4  (residues 1 to 332)
  AUTHORS   Vetterkind,S., Illenberger,S., Kubicek,J., Boosen,M., Appel,S.,
            Naim,H.Y., Scheidtmann,K.H. and Preuss,U.
  TITLE     Binding of Par-4 to the actin cytoskeleton is essential for
            Par-4/Dlk-mediated apoptosis
  JOURNAL   Exp. Cell Res. 305 (2), 392-408 (2005)
   PUBMED   15817164
  REMARK    INTERACTION WITH ACTIN.
```

COMMENT [FUNCTION] Pro-apoptopic protein capable of selectively inducing apoptosis in cancer cells, sensitizing the cells to diverse apoptotic stimuli and causing regression of tumors in animal models. Induces apoptosis in certain cancer cells by activation of the Fas prodeath pathway and coparallel inhibition of NF-kappa-B transcriptional activity. Inhibits the transcriptional activation and augments the transcriptional repression mediated by WT1. Down-regulates the anti-apoptotic protein BCL2 via its interaction with WT1. Seems also to be a transcriptional repressor by itself. May be directly involved in regulating the amyloid precursor protein (APP) cleavage activity of BACE1 (By similarity).
[SUBUNIT] Interacts with WT1, via the C-terminal region. Homooligomer. Interacts also with a wide variety of proteins, such as atypical PKCs, p62, DAPK3 kinase and THAP1. Interacts with actin, AATF, BACE1, SPSB1, SPSB2 AND SPSB4. Component of a ternary complex composed of SQSTM1 and PRKCZ (By similarity).
[SUBCELLULAR LOCATION] Cytoplasm (By similarity). Nucleus (By similarity). Note=Mainly cytoplasmic in absence of apoptosis signal and in normal cells. Nuclear in most cancer cell lines. Nuclear entry seems to be essential but not sufficient for apoptosis. Nuclear localization includes nucleoplasm and PML nuclear bodies (By similarity).
[INDUCTION] In ventral prostate following castration.
[DOMAIN] The leucine-zipper domain is not essential for apoptosis, but is required for sensitization of cells to exogenous apoptotic insults and for interaction with its partners (By similarity).
[DOMAIN] The SAC domain is a death-inducing domain selective for apoptosis induction in cancer cells. This domain is essential for nuclear entry, Fas activation, inhibition of NF-kappa-B activity and induction of apoptosis in cancer cells (By similarity).
[PTM] Preferentially phosphorylated at the Thr-155 by PKC in cancer cells.

FEATURES Location/Qualifiers

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/db_xref="taxon:10116"

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Region 137..153
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Site 155
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Region 176..198
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/region_name="Coiled-coil region"

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